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=> fil hcaplu
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FILE COVERS 1907 - 28 Apr 2003  VOL 138 ISS 18
FILE LAST UPDATED: 27 Apr 2003  (20030427/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


=> d stat que
L1          391 SEA FILE=REGISTRY WNT/BI
L3            3 SEA FILE=REGISTRY ("WNT7A-PROTEIN (RATTUS NORVEGICUS STRAIN
                  WISTAR C-TERMINAL FRAGMENT)"/CN OR "WNT7B PROTEIN (HUMAN GENE
                  WNT7B)"/CN)
L4         2474 SEA FILE=HCAPLUS L1 OR WNT
L5            1 SEA FILE=REGISTRY "SULFATED GLYCOSAMINOGLYCANS"/CN
L6            6 SEA FILE=REGISTRY HLDAT86/BI
L8           68 SEA FILE=HCAPLUS L3 OR WNT4
L9         1254 SEA FILE=HCAPLUS L5 OR SULFATED(W)GLYCOSAMINOGLYCAN?
L10           2 SEA FILE=HCAPLUS L6 OR HLDAT86
L11         172 SEA FILE=HCAPLUS (L4 OR L8 OR L10) AND (KIDNEY? OR RENAL? OR
                  NEPHROPATH? OR UROPATH? OR HIV(W)1 OR HIV1)
L12          41 SEA FILE=HCAPLUS L11 AND TUBUL?
L13           1 SEA FILE=HCAPLUS L12 AND L9


=> d ibib abs hitrn l13

L13  ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2003 ACS
ACCESSION NUMBER:         1998:802909  HCAPLUS
DOCUMENT NUMBER:          130:137130
TITLE:                    Wnt-4 is a mesenchymal signal for epithelial
                          transformation of metanephric mesenchyme in the
                          developing kidney
AUTHOR(S):                Kispert, Andreas; Vainio, Seppo; McMahon, Andrew P.
CORPORATE SOURCE:         Department of Molecular and Cellular Biology, Harvard
                          University, Cambridge, MA, 02138, USA
SOURCE:                   Development (Cambridge, United Kingdom) (1998),
                          125(21), 4225-4234
                          CODEN: DEVPED; ISSN: 0950-1991
PUBLISHER:                Company of Biologists Ltd.
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB   Development of the mammalian kidney is initiated by ingrowth of
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the ureteric bud into the metanephric blastema. In response to signal(s) from the ureter, mesenchymal cells condense, aggregate into pretubular clusters, and undergo epithelialization to form simple epithelial **tubules**. Subsequent morphogenesis and differentiation of the **tubular** epithelium leads to the establishment of a functional nephron. Here, we demonstrate that **Wnt**-4, a secreted glycoprotein which is required for **tubule** formation, is sufficient to trigger **tubulogenesis** in isolated metanephric mesenchyme, whereas **Wnt**-11 which is expressed in the tip of the growing ureter is not. **Wnt**-4 signaling depends on cell contact and **sulfated glycosaminoglycans** and is only required for triggering **tubulogenesis** but not for later events. The **Wnt**-4 signal can be replaced by other members of the **Wnt** gene family including **Wnt**-1, **Wnt**-3a, **Wnt**-7a and **Wnt**-7b. Further, dorsal spinal cord, which has been thought to mimic ureteric signaling in **tubule** induction induces **Wnt**-4 mutant as well as wild-type mesenchyme suggesting that spinal cord derived signal(s) most likely act by mimicking the normal mesenchymal action of **Wnt**-4. These results lend addnl. support to the notion that **Wnt**-4 is a key auto-regulator of the mesenchymal to epithelial transformation that underpins nephrogenesis adding another level of complexity in the hierarchy of mol. events mediating **tubulogenesis**.

REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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=> d stat que l14
L1          391 SEA FILE=REGISTRY WNT/BI
L3            3 SEA FILE=REGISTRY ("WNT7A-PROTEIN (RATTUS NORVEGICUS STRAIN
                WISTAR C-TERMINAL FRAGMENT)"/CN OR "WNT7B PROTEIN (HUMAN GENE
                WNT7B)"/CN)
L4         2474 SEA FILE=HCAPLUS L1 OR WNT
L6            6 SEA FILE=REGISTRY HLDAT86/BI
L8           68 SEA FILE=HCAPLUS L3 OR WNT4
L10           2 SEA FILE=HCAPLUS L6 OR HLDAT86
L14          22 SEA FILE=HCAPLUS KIDNEY?(5A)TUBUL? AND (L4 OR L8 OR L10)


=> d ibib abs hitrn l14 1-22

L14  ANSWER 1 OF 22  HCAPLUS  COPYRIGHT 2003 ACS
ACCESSION NUMBER:        2003:81353  HCAPLUS
TITLE:                   Nuclear accumulation of .beta.-catenin protein in
                         Wilms' tumours
AUTHOR(S):               Koesters, Robert; Niggli, Felix; von Knebel Doeberitz,
                         Magnus; Stallmach, Thomas
CORPORATE SOURCE:        Division of Molecular Pathology, Department of
                         Pathology, University Hospital of Heidelberg,
                         Heidelberg, Germany
SOURCE:                  Journal of Pathology (2003), Volume Date 2002, 199(1),
                         68-76
                         CODEN: JPTLAS; ISSN: 0022-3417
PUBLISHER:               John Wiley & Sons Ltd.
DOCUMENT TYPE:           Journal
LANGUAGE:                English
AB   The wnt-signalling pathway plays an important role during both
     normal kidney development and Wilms' tumorigenesis. Activation of this
     pathway involves stabilization, intracellular accumulation, and nuclear
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translocation of the .beta.-catenin protein and may be caused by specific mutations in the .beta.-catenin gene itself. Such mutations have been found in about 15% of Wilms' tumors. This study has analyzed the intracellular levels and subcellular distribution of .beta.-catenin protein in 36 primary Wilms' tumor specimens and has correlated these results with the mutational status of the .beta.-catenin gene. Immunohistochem. detected faint cytoplasmic and strong membranous expression of .beta.-catenin protein in the epithelial compartment of all tumors examd. In contrast, nuclear immunoreactivity for .beta.-catenin was detected in 9 of 9 Wilms' tumors contg. a mutation of the .beta.-catenin gene and in 15 of 27 Wilms' tumors without detectable .beta.-catenin mutation. Nuclear positivity, in each case, was found to be very strong, but was usually present only in a fraction of cells ranging from 5% to 10%. Among the different histol. subcompartments, blastemal and mesenchymal cell nuclei preferentially stained pos., whereas cells of epithelial differentiation displayed nuclear localization of .beta.-catenin protein in only a single case. Furthermore, nuclear pos. cells were found in Wilms' tumors of all stages and in tumors of both favorable and unfavorable histol. These data support the idea that activation of the **wnt**-signalling pathway is a key oncogenic step in Wilms' tumorigenesis and that it probably involves transcriptional activation of crit. target genes, carried out by .beta.-catenin protein in the nucleus. The fact that nuclear immunoreactivity specific for .beta.-catenin was detected in a significant no. of Wilms' tumors in the absence of .beta.-catenin mutations suggests that genetic defects affecting other members of the **wnt**-signalling pathway may contribute to the development of Wilms' tumors in those cases.

REFERENCE COUNT: 58 THERE ARE 58 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 2 OF 22 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:870450 HCAPLUS
DOCUMENT NUMBER: 138:219603
TITLE: Involvement of Pax-2 in the Action of Activin A on Tubular Cell Regeneration
AUTHOR(S): Maeshima, Akito; Maeshima, Kyoko; Nojima, Yoshihisa; Kojima, Itaru
CORPORATE SOURCE: Institute for Molecular and Cellular Regulation, Gunma University, Maebashi, Japan
SOURCE: Journal of the American Society of Nephrology (2002), 13(12), 2850-2859
CODEN: JASNEU; ISSN: 1046-6673
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB It has been recently shown that in ischemic rat **kidneys** activin A is induced in **tubular** cells and inhibits their regeneration. The present study was conducted to further investigate the action of activin A in tubular cells during regeneration. Among genes thought to be crit. for kidney development, Pax-2 was upregulated in tubular cells during regeneration after renal ischemia. Pax-2 protein was localized in nuclei of tubular and interstitial cells, some of which co-expressed a mesenchymal cell marker, vimentin, suggesting that a population of Pax-2-pos. cells have properties of immature progenitor-like tubular cells. The Pax-2-expressing cells co-expressed a cell proliferation marker, BrdU, activin A, and the type II activin receptor. Activin A modulated growth of BrdU/Pax-2 double-pos. cells since an administration of follistatin increased; conversely, exogenous activin A decreased the no. of BrdU/Pax-2 double-pos. cells after renal ischemia. Activin A also

reduced the expression of Pax-2 in cultured metanephroi. A proximal tubular cell line, LLC-PK1 cells, was used to further study the mode of action of activin A. The expression of Pax-2 was not detected in quiescent LLC-PK1 cells, but it was markedly increased when growth was stimulated. Under this condition, activin A significantly inhibited DNA synthesis and reduced the expression of Pax-2 in LLC-PK1 cells. In contrast, blockade of the activin signaling by overexpressing dominantly neg. mutant receptor enhanced the expression level of Pax-2 in LLC-PK1 cells and induced an immature phenotype. These results suggest that activin A regulates tubular cell growth and differentiation by modulating the expression of Pax-2 during regeneration.

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 3 OF 22 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:869218 HCAPLUS
DOCUMENT NUMBER: 137:364363
TITLE: Screening method for identifying biological active agents against specific cellular targets
INVENTOR(S): Andrews, Peter; Draper, Jon; Walsh, James
PATENT ASSIGNEE(S): Axordia Ltd., UK
SOURCE: PCT Int. Appl., 90 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002090992	A2	20021114	WO 2002-GB1946	20020429

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 2001-11004 A 20010504

AB The invention provides a novel screening method which enables the identification of biol. active agents which mediate their effects through the activation of genes. The method utilizes promoter trap, enhancer trap and gene trap constructs, comprising a reporter mol., which are transfected into cells which are then cloned into a cell array. The cell array is exposed to an agent(s) to be tested and the response of the cell array to the agent monitored. The method enables both the identification of agents and the genes through which the agents act.

IT **475440-20-1P**, Protein **Wnt**-1 (synthetic)
475440-22-3P, Protein **Wnt**-2 (synthetic)
475440-24-5P, Protein **Wnt**-2B (synthetic)
475440-26-7P, Protein **Wnt**-3 (synthetic)
475440-28-9P, Protein **Wnt**-4 (synthetic)
475440-30-3P, Protein **Wnt**-5A (synthetic)
475440-32-5P, Protein **Wnt**-6 (synthetic)
475440-34-7P, Protein **Wnt**-7A (synthetic)
475440-35-8P, Protein **Wnt**-7B (synthetic)

475440-37-0P, Protein **Wnt**-8B (synthetic)
475440-39-2P, Protein **Wnt**-10B (synthetic)
475440-41-6P, Protein **Wnt**-11 (synthetic)
475440-43-8P, Protein **Wnt**-14 (synthetic)
475440-45-0P, Protein **Wnt**-16 (synthetic)
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation)
(amino acid sequence; screening method for identifying biol. active agents against specific cellular targets)

IT **475440-14-3 475440-19-8 475440-21-2**
475440-23-4 475440-25-6 475440-27-8
475440-29-0 475440-31-4 475440-33-6
475440-36-9 475440-38-1 475440-40-5
475440-42-7 475440-44-9
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(nucleotide sequence; screening method for identifying biol. active agents against specific cellular targets)

L14 ANSWER 4 OF 22 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:736423 HCAPLUS
DOCUMENT NUMBER: 137:274009
TITLE: Cell-specific gene expression profiles and algorithms for their construction and their uses for determining the phenotype of cells and distinguishing cell lines
INVENTOR(S): Wan, Jackson; Wang, Yixin
PATENT ASSIGNEE(S): Ortho-Clinical Diagnostics, Inc., USA
SOURCE: PCT Int. Appl., 850 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002074979	A2	20020926	WO 2002-US8456	20020320
WO 2002074979	A3	20030313		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-276947P P 20010320

AB The present invention relates to gene expression profiles, algorithms to generate gene expression profiles, microarrays comprising nucleic acid sequences representing gene expression profiles, methods of using gene expression profiles and microarrays, and business methods directed to the use of gene expression profiles, microarrays, and algorithms. By integrating laser capture microdissection, RNA amplification, and cDNA microarray technol., diverse cell types obtained in situ may be successfully screened and subsequently identified by differential gene expression. To demonstrate this integration of technologies, the differential gene expressions of large and small-sized neurons in the dorsal root ganglia of rats were examd., and 477 cDNAs identified with

1.5-fold or greater differences. The gene expression data is transformed into a log-ratio value, and the genes with weak differential values are filtered from the data; the gene expression profiles are then extd. using the MaxCor or Mean Log Ratio algorithms of the present invention. For an unknown sample, it may be necessary to transform the gene expression data of the sample prior to scoring against the expression profiles. Gene expression profiles were thus collected from a set of human primary cells via DNA microarray technol. Cluster anal. of 803 nucleic acid sequences confirmed that the samples could be classified into 3 groups: endothelial, epithelial, and muscle cell.

IT **392081-73-1**, DNA (human **Wnt** inhibitory factor-1 cDNA)
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(nucleotide sequence; cell-specific gene expression profiles and algorithms for their construction and their uses for detg. the phenotype of cells and distinguishing cell lines)

L14 ANSWER 5 OF 22 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:556221 HCAPLUS
DOCUMENT NUMBER: 137:276041
TITLE: Essential function of **Wnt**-4 for **tubulogenesis** in the Xenopus pronephric **kidney**
AUTHOR(S): Saulnier, Didier M. E.; Ghanbari, Hedyeh; Braendli, Andre W.
CORPORATE SOURCE: Department of Applied Biosciences, Swiss Federal Institute of Technology (ETHZ), Zurich, CH-8057, Switz.
SOURCE: Developmental Biology (Orlando, FL, United States) (2002), 248(1), 13-28
CODEN: DEBIAO; ISSN: 0012-1606
PUBLISHER: Elsevier Science
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In the vertebrate embryo, development of the excretory system is characterized by the successive formation of 3 distinct kidneys: the pronephros, mesonephros, and metanephros. While **tubulogenesis** in the metanephric **kidney** is critically dependent on the signaling mol. **Wnt**-4, it is unknown whether **Wnt** signaling is equally required for the formation of renal epithelia in the other embryonic kidney forms. We therefore investigated the expression of **Wnt** genes during the pronephric kidney development in Xenopus. **Wnt4** was found to be assocd. with developing pronephric tubules, but was absent from the pronephric duct. Onset of pronephric **Wnt**-4 expression coincided with mesenchyme-to-epithelium transformation. To investigate **Wnt**-4 gene function, we performed gain- and loss-of-function expts. Misexpression of **Wnt4** in the intermediate and lateral mesoderm caused abnormal morphogenesis of the pronephric tubules, but was not sufficient to initiate ectopic tubule formation. We used a morpholino antisense oligonucleotide-based gene knockdown strategy to disrupt **Wnt**-4 gene function. Xenopus embryos injected with antisense **Wnt**-4 morpholinos developed normally, but marker gene and morphol. anal. revealed a complete absence of pronephric tubules. Pronephric duct development was largely unaffected, indicating that ductogenesis may occur normally in the absence of pronephric tubules. Our results show that, as in the metanephric kidney, **Wnt**-4 is critically required for **tubulogenesis** in the pronephric **kidney**, indicating that a common, evolutionary conserved gene regulatory network may control tubulogenesis in different

vertebrate excretory organs.
REFERENCE COUNT: 70 THERE ARE 70 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 6 OF 22 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:420004 HCAPLUS
DOCUMENT NUMBER: 137:349731
TITLE: **Wnt**-6 is expressed in the ureter bud and induces **kidney tubule** development in vitro
AUTHOR(S): Itaranta, Petri; Lin, Yanfeng; Perasaari, Juha; Roel, Giulietta; Destree, Olivier; Vainio, Seppo
CORPORATE SOURCE: Biocenter Oulu, Department of Biochemistry, University of Oulu, Oulu, 90570, Finland
SOURCE: Genesis (New York, NY, United States) (2002), 32(4), 259-268
CODEN: GNESFY; ISSN: 1526-954X
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The embryonic kidney is a classic developmental model system for studying inductive tissue interactions that govern organogenesis. The authors report here that **Wnt**-6 is expressed in the ureter bud, and that cell lines expressing **Wnt**-6 induce nephrogenesis in vitro. **Wnt**-6 cells induce tubules with similar kinetics to spinal cord (SPC) and lead to induced expression of Pax2, Pax8, Sfrp2, and E-cadherin genes, early markers of tubulogenesis. Moreover, **Wnt**-6 signaling rescues tubulogenesis in mesenchyme sepd. from **Wnt**-4 mutant embryos and leads to activation of **Wnt**-4 transcription. **Wnt**-6 also induces a secondary axis in early Xenopus embryos. The authors conclude that **Wnt**-6 is a candidate for the ureter epithelium-derived signal that leads to activation of **kidney tubulogenesis** via **Wnt**-4.
REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 7 OF 22 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:412131 HCAPLUS
DOCUMENT NUMBER: 137:245049
TITLE: ATP depletion of tubular cells causes dissociation of the zonula adherens and nuclear translocation of .beta.-catenin and LEF-1
AUTHOR(S): Price, Valerie R.; Reed, Christine A.; Lieberthal, Wilfred; Schwartz, John H.
CORPORATE SOURCE: Renal Section, Boston University School of Medicine, Boston, MA, USA
SOURCE: Journal of the American Society of Nephrology (2002), 13(5), 1152-1161
CODEN: JASNEU; ISSN: 1046-6673
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB This study examd. the events assocd. with the reversible disruption of the structural and functional integrity of the zonula occludens (ZA) induced by ATP depletion of renal tubular cells. It shows that loss of the ZA after ATP depletion is assocd. with the withdrawal of E-cadherin, .alpha.-catenin, and .beta.-catenin, probably as intact cadherin-catenin complexes from the basolateral membrane of tubular cells. The relative amts. of all three proteins increased in the Triton X-100-insol. fraction

of cell lysates and decreased in the Triton X-100-sol. pool. These changes were reversed with repletion of cell ATP. It is addnl. shown that ATP depletion induces nuclear translocation of .beta.-catenin and T cell factor (TCF)/lymphoid enhancer factor-1 (LEF-1), a transcriptional factor with which .beta.-catenin assocs. The redistribution of the ZA proteins as intact E-cadherin-catenin complexes from the plasma membrane facilitates the rapid recovery of the ZA after sublethal ischemic injury. The translocation of .beta.-catenin and TCF/LEF-1 to the nucleus indicates that ATP depletion may activate the **wnt**/wingless signal transduction pathway. Thus, entirely novel evidence is provided that both of the known roles of .beta.-catenin, as a structural part of the ZA and as a component of the **wnt**/wingless pathway, play a role after sublethal ischemic injury to tubular cells. It is also speculated that the nuclear translocation of .beta.-catenin and TCF/LEF-1 modulates gene expression after ischemic injury and may contribute to events necessary for renal regeneration and repair after ischemic injury.

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 8 OF 22 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:225356 HCAPLUS
DOCUMENT NUMBER: 136:384300
TITLE: A role for **Wnt**-4 in renal fibrosis
AUTHOR(S): Surendran, Kameswaran; McCaul, Sean P.; Simon, Theodore C.
CORPORATE SOURCE: Department of Pediatrics Division of Biology and Biomedical Sciences, Washington University School of Medicine, St. Louis, MO, 63110, USA
SOURCE: American Journal of Physiology (2002), 282(3, Pt. 2), F431-F441
CODEN: AJPHAP; ISSN: 0002-9513
PUBLISHER: American Physiological Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Wnt**-4 is a secreted glycoprotein that is crit. for genitourinary development but found only in the most distal collecting duct epithelium in the normal murine adult kidney. **Wnt4** expression is induced throughout the collecting ducts in four murine models of renal injury that produce tubulointerstitial fibrosis: folic acid-induced nephropathy, unilateral ureteral obstruction, renal needle puncture, and genetic polycystic kidney disease. **Wnt4** activation induced by injury is limited to collecting ducts, with initial activation in the collecting duct epithelium followed by activation in fibrotic lesions surrounding the collecting ducts. The highest cellular **Wnt4** expression is in interstitial fibroblasts in the fibrotic lesions that also express high levels of collagen-.alpha.1(I) mRNA and .alpha.-smooth muscle actin. In support of a functional role for **Wnt**-4 in these activated myofibroblasts, **Wnt**-4 induces stabilization of cytosolic .beta.-catenin in a cultured myofibroblast cell line. Furthermore, **Wnt**-4-producing fibroblasts placed under the renal capsule of adult mice induce lesions with tubular epithelial destruction. These observations suggest a role for **Wnt**-4 in the pathogenesis of renal fibrosis.

REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 9 OF 22 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:744020 HCAPLUS
DOCUMENT NUMBER: 136:35844

TITLE: Early development of polycystic kidney disease in transgenic mice expressing an activated mutant of the .beta.-catenin gene
AUTHOR(S): Saadi-Kheddouci, Sihem; Berrebi, Dominique; Romagnolo, Beatrice; Cluzeaud, Francoise; Peuchmaur, Michel; Kahn, Axel; Vandewalle, Alain; Perret, Christine
CORPORATE SOURCE: INSERM U129, ICGM, Paris, 75014, Fr.
SOURCE: Oncogene (2001), 20(42), 5972-5981
CODEN: ONCNES; ISSN: 0950-9232
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Autosomal dominant polycystic kidney disease (ADPKD) is common and is a major cause of renal failure. Although the genetics of ADPKD are well known and have led to the discovery of polycysteins, a new protein family, the pathogenesis of the disease remains largely unknown. Recent studies have indicated that the .beta.-catenin signaling pathway is one of the targets of the transduction pathway controlled by the polycystins. We have generated transgenic mice that overproduce an oncogenic form of .beta.-catenin in the epithelial cells of the kidney. These mice developed severe polycystic lesions soon after birth that affected the glomeruli, proximal, distal tubules and collecting ducts. The phenotype of these mice mimicked the human ADPKD phenotype. Cyst formation was assocd. with an increase in cell proliferation and apoptosis. The cell proliferation and apoptotic indexes was increased 4-5-fold and 3-4-fold, resp., in cystic tubules of the transgenic mice compared to that of littermate controls. Our findings provide exptl. genetic evidence that activation of the **Wnt**/.beta.-catenin signaling pathway causes polycystic kidney disease and support the view that dysregulation of the **Wnt**/.beta.-catenin signaling is involved in its pathogenesis.
REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 10 OF 22 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:670806 HCAPLUS
DOCUMENT NUMBER: 135:369563
TITLE: Murine homolog of SALL1 is essential for ureteric bud invasion in kidney development
AUTHOR(S): Nishinakamura, Ryuichi; Matsumoto, Yuko; Nakao, Kazuki; Nakamura, Kenji; Sato, Akira; Copeland, Neal G.; Gilbert, Debra J.; Jenkins, Nancy A.; Scully, Sheila; Lacey, David L.; Katsuki, Motoya; Asashima, Makoto; Yokota, Takashi
CORPORATE SOURCE: Division of Stem Cell Regulation, Institute of Medical Science, The University of Tokyo, Tokyo, 108-8639, Japan
SOURCE: Development (Cambridge, United Kingdom) (2001), 128(16), 3105-3115
CODEN: DEVPED; ISSN: 0950-1991
PUBLISHER: Company of Biologists Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB SALL1 is a mammalian homolog of the Drosophila region-specific homeotic gene spalt (sal); heterozygous mutations in SALL1 in humans lead to Townes-Brocks syndrome. We have isolated a mouse homolog of SALL1 (Sall1) and found that mice deficient in Sall1 die in the perinatal period and that kidney agenesis or severe dysgenesis are present. Sall1 is expressed in the metanephric mesenchyme surrounding ureteric bud; homozygous deletion of Sall1 results in an incomplete ureteric bud outgrowth, a

failure of tubule formation in the mesenchyme and an apoptosis of the mesenchyme. This phenotype is likely to be primarily caused by the absence of the inductive signal from the ureter, as the Sall1-deficient mesenchyme is competent with respect to epithelial differentiation. Sall1 is therefore essential for ureteric bud invasion, the initial key step for metanephros development.

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 11 OF 22 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:607244 HCAPLUS
DOCUMENT NUMBER: 135:301479
TITLE: **Wnt** signaling in human development: Beta-catenin nuclear translocation in fetal lung, kidney, placenta, capillaries, adrenal, and cartilage
AUTHOR(S): Eberhart, Charles G.; Argani, Pedram
CORPORATE SOURCE: Department of Pathology, Johns Hopkins School of Medicine, Baltimore, MD, 21287, USA
SOURCE: Pediatric and Developmental Pathology (2001), 4(4), 351-357
CODEN: PDPAFU; ISSN: 1093-5266
PUBLISHER: Springer-Verlag New York Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The **Wnt** signaling pathway is involved in both normal development and tumorigenesis. Activation of the pathway results in stabilization and nuclear translocation of beta-catenin protein. Nuclear localization of beta-catenin has been used to identify tumors in which mutations in APC or beta-catenin activate **Wnt** signaling. We analyzed the subcellular localization of beta-catenin immunohistochem. in human fetal and postnatal tissues to identify activation of **Wnt** signaling during development. Nuclear beta-catenin is present in capillary endothelium, mesenchyme surrounding renal tubules, adrenal cortex, cartilage anlage, placental cytotrophoblast, and pulmonary acinar buds. These investigations suggest a defined role for **Wnt** signaling in human fetal development and provide a catalog of non-neoplastic tissues with nuclear beta-catenin staining.
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 12 OF 22 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:564849 HCAPLUS
DOCUMENT NUMBER: 135:132443
TITLE: Method using a Pax2 expression enhancer for treating kidney disorders
INVENTOR(S): Rothenpieler, Uwe Waldemar; Imgrund, Michael Carl Elmar
PATENT ASSIGNEE(S): Germany
SOURCE: PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001054706	A2	20010802	WO 2001-EP1004	20010131
WO 2001054706	A3	20020124		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1255569 A2 20021113 EP 2001-921268 20010131
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRIORITY APPLN. INFO.: US 2000-179129P P 20000131
WO 2001-EP1004 W 20010131

AB A method is provided for treating, delaying, and/or preventing renal dysfunction/failure in a mammal which comprises administering a therapeutically effective amt. of a substance capable of inducing and/or enhancing Pax2 expression. The invention further relates to the use of an ED of a substance capable of inducing and/or enhancing Pax2 expression in a mammal for the prepn. of a pharmaceutical compn. for treating, preventing or delaying a renal dysfunction/failure in a mammal. Also provided are a method for converting mesenchymal tissue into an epithelial tissue, comprising the administration of an effective amt. of a substance capable of inducing and/or enhancing Pax2 expression in the mesenchyme , and a method for the regeneration of renal stem cells comprising the administration of an effective amt. of a substance capable of inducing and/or enhancing Pax2 expression.

L14 ANSWER 13 OF 22 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:842971 HCAPLUS
DOCUMENT NUMBER: 134:263769
TITLE: Secreted molecules in metanephric induction
AUTHOR(S): Carroll, Thomas J.; McMahon, Andrew P.
CORPORATE SOURCE: Department of Molecular and Cellular Biology, Biological Laboratories, Harvard University, Cambridge, MA, 02138, USA
SOURCE: Journal of the American Society of Nephrology (2000), 11(11, Suppl. 16), S116-S119
CODEN: JASNEU; ISSN: 1046-6673
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 21 refs. Nearly 50 yr ago, Clifford Grobstein made the observation that the ureteric bud induced the nephrogenic mesenchyme to undergo tubulogenesis. Since that discovery, scientists have attempted to characterize the mol. nature of the inducer. To date, no single mol. that is both necessary and sufficient for nephric induction was identified. Because of recent insights regarding the role of several secreted mols. in tubulogenesis, it has become necessary to revise the classic model of metanephric induction. The studies of the classic ureteric inducer performed to date have most likely been characterizations of a mesenchyme-specific inducer, **Wnt**-4, and its role in tubulogenesis. Ureteric induction most likely involves a series of distinct events that provide proliferative, survival, and condensation signals to the mesenchyme, integrating the growth of the ureteric system with tubulogenesis.

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 14 OF 22 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:742138 HCAPLUS
DOCUMENT NUMBER: 133:305599
TITLE: Induction of **kidney tubule** formation
INVENTOR(S): Mcmahon, Andrew P.; Kispert, Andreas; Vainio, Seppo
PATENT ASSIGNEE(S): President and Fellows of Harvard College, USA
SOURCE: PCT Int. Appl., 53 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000061630	A1	20001019	WO 1999-US7745	19990408

W: CA, JP, US
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
PRIORITY APPLN. INFO.: WO 1999-US7745 19990408
AB The invention provides a method of stimulating **kidney tubule** formation in a post-natal mammal by administering to the mammal a substantially pure **Wnt** polypeptide or **Wnt** agonist.
IT **302450-60-8**, Glycoprotein (human gene **Wnt**-3a)
302450-61-9, Glycoprotein (human gene **Wnt**-4)
302450-62-0, Glycoprotein (human gene **Wnt**-7a)
302450-63-1, Glycoprotein (human gene **Wnt**-7b)
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amino acid sequence; induction of **kidney tubule** formation by administering **Wnt** polypeptide or **Wnt** agonist)
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 15 OF 22 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:446404 HCAPLUS
DOCUMENT NUMBER: 133:162087
TITLE: Colocalization and redistribution of dishevelled and actin during **Wnt**-induced mesenchymal morphogenesis
AUTHOR(S): Torres, Monica A.; Nelson, W. James
CORPORATE SOURCE: Department of Molecular and Cellular Physiology, Stanford University School of Medicine, Stanford, CA, 94305-5345, USA
SOURCE: Journal of Cell Biology (2000), 149(7), 1433-1442
CODEN: JCLBA3; ISSN: 0021-9525
PUBLISHER: Rockefeller University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Activation of the **Wnt** signaling pathway is important for induction of gene expression and cell morphogenesis throughout embryonic development. We examd. the subcellular localization of dishevelled, the immediate downstream component from the **Wnt** receptor, in the embryonic mouse kidney. Using immunofluorescence staining, confocal microscopy, and coimmunopptn. expts., we show that dishevelled assocs.

with actin fibers and focal adhesion plaques in metanephric mesenchymal cells. Stimulation of **Wnt** signaling leads to profound changes in metanephric mesenchymal cell morphol., including disruption of the actin cytoskeleton, increased cell spreading, and increased karyokinesis. Upon activation of **Wnt** signaling, dishevelled also accumulates in and around the nucleus. Casein kinase I.epsilon. colocalizes with dishevelled along actin fibers and in the perinuclear region, whereas axin and GSK-3 are only present around the nucleus. These data indicate a branched **Wnt** signaling pathway comprising a canonical signal that targets the nucleus and gene expression, and another signal that targets the cytoskeleton and regulates cell morphogenesis.

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 16 OF 22 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:305583 HCAPLUS
DOCUMENT NUMBER: 132:305479
TITLE: Methods and compositions for growth of **kidney tubule** stem cells, in vitro **kidney tubulogenesis** and ex vivo construction of renal tubules
INVENTOR(S): Humes, H. David
PATENT ASSIGNEE(S): The University of Michigan, USA
SOURCE: U.S., 17 pp., Cont.-in-part of U.S. 5,429,938.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6060270	A	20000509	US 1995-449912	19950525
US 2002119566	A1	20020829	US 2002-82261	20020226

PRIORITY APPLN. INFO.: US 1992-844758 A2 19920302
US 1995-449912 A1 19950525
US 2000-494044 A1 20000131

AB Methods, including culture media conditions, for growing renal tubule stem cells ex vivo, for in vitro **kidney tubulogenesis**, for constructing and maintaining ex vivo renal tubule tissue system, and for expressing therapeutically useful polypeptide in a renal tubule tissue system are disclosed. The methods rely on culturing adult kidney cells in a culture media contg. combinations of transforming growth factor-.beta.1 (TGF-.beta.1), all-trans retinoic acid (RA), and either epidermal growth factor (EGF) or transforming growth factor-.alpha. (TGF-.alpha.). The culture media contains sol. factors such as fetal calf serum, prostaglandins, hydrocortisone, triiodothyronine, selenium, fibroblastic growth factor, hepatocyte growth factor, insulin-like growth factor I, **Wnt**-1, and **Wnt**-4, and insol. factors such as Type I collagen, Type IV collagen, laminin, proteoglycans, and fibronectin. The culture media may also contain adhesion mols. such as cell attachment sequence from human fibronectin and epitope from laminin alpha chain. Adult rabbit renal proximal tubule cells grown in culture media supplemented with EGF and RA underwent transformation of the monolayer into adherent cell aggregates with defined tubular lumen structure. Progressive passage of cells promoted increasingly more defined tubular structures.

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 17 OF 22 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:771977 HCAPLUS
DOCUMENT NUMBER: 132:163810
TITLE: Wnts as **kidney tubule** inducing factors
AUTHOR(S): Vainio, Seppo J.; Itaranta, Petri V.; Perasaari, Juha P.; Uusitalo, Marika S.
CORPORATE SOURCE: Biocenter Oulu and Department of Biochemistry, University of Oulu, Oulu, 90570, Finland
SOURCE: International Journal of Developmental Biology (1999), 43(5, Spec. Issue), 419-423
CODEN: IJDBE5; ISSN: 0214-6282
PUBLISHER: University of the Basque Country Press
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 20 refs. Since the discovery that inductive tissue interactions regulate nephrogenesis, one of the aims has been to identify the mols. that mediate this induction. The small size of embryonic tissue has limited the possibilities to identify the inducers biochem., even though such efforts were directed to study, e.g. neural induction (for a comprehensive review, Saxen and Toivonen, Primary embryonic induction, Academic Press, London, 1962). The rapid progress in mol. biol. made it possible to identify genes from minute amts. of tissue and provided techniques to generate recombinant proteins to assay their action in classic exptl. systems. This led to the identification of some signals that are involved in primary and secondary inductive interactions during embryogenesis. Here, we will review evidence suggesting that secreted signaling mols. from the **Wnt** gene family mediate **kidney tubule** induction.
REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 18 OF 22 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:150620 HCAPLUS
DOCUMENT NUMBER: 130:292388
TITLE: The polycystic kidney disease 1 gene product modulates **Wnt** signaling
AUTHOR(S): Kim, Emily; Arnould, Thierry; Sellin, Lorenz K.; Benzing, Thomas; Fan, Melinda J.; Gruning, Wolfram; Sokol, Sergei Y.; Drummond, Iain; Walz, Gerd
CORPORATE SOURCE: Laboratory of Molecular and Developmental Neuroscience, Harvard Medical School, Massachusetts General Hospital, Boston, MA, 02114, USA
SOURCE: Journal of Biological Chemistry (1999), 274(8), 4947-4953
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Two distinct signaling pathways, involving **Wnt** signaling and polycystin, have been found to be crit. for normal kidney development. Renal tubulogenesis requires the presence of certain **Wnt** proteins, whereas mutations in polycystin impede the terminal differentiation of renal tubular epithelial cells, causing the development of large cystic kidneys that characterize autosomal dominant polycystic kidney disease. Polycystin is an integral membrane protein, consisting of several extracellular motifs indicative of cell-cell and cell-matrix

interactions, coupled through multiple transmembrane domains to a functionally active cytoplasmic domain. We report here that expression of the C-terminal cytoplasmic domain of polycystin stabilizes sol. endogenous .beta.-catenin and stimulates TCF-dependent gene transcription in human embryonic kidney cells. Microinjection of the polycystin C-terminal cytoplasmic domain induces dorsalization in zebrafish. Our findings suggest that polycystin has the capacity to modulate **Wnt** signaling during renal development.

REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 19 OF 22 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:802909 HCAPLUS
DOCUMENT NUMBER: 130:137130
TITLE: **Wnt**-4 is a mesenchymal signal for epithelial transformation of metanephric mesenchyme in the developing kidney
AUTHOR(S): Kispert, Andreas; Vainio, Seppo; McMahon, Andrew P.
CORPORATE SOURCE: Department of Molecular and Cellular Biology, Harvard University, Cambridge, MA, 02138, USA
SOURCE: Development (Cambridge, United Kingdom) (1998), 125(21), 4225-4234
CODEN: DEVPED; ISSN: 0950-1991
PUBLISHER: Company of Biologists Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Development of the mammalian kidney is initiated by ingrowth of the ureteric bud into the metanephric blastema. In response to signal(s) from the ureter, mesenchymal cells condense, aggregate into pretubular clusters, and undergo epithelialization to form simple epithelial tubules. Subsequent morphogenesis and differentiation of the tubular epithelium leads to the establishment of a functional nephron. Here, we demonstrate that **Wnt**-4, a secreted glycoprotein which is required for tubule formation, is sufficient to trigger tubulogenesis in isolated metanephric mesenchyme, whereas **Wnt**-11 which is expressed in the tip of the growing ureter is not. **Wnt**-4 signaling depends on cell contact and sulfated glycosaminoglycans and is only required for triggering tubulogenesis but not for later events. The **Wnt**-4 signal can be replaced by other members of the **Wnt** gene family including **Wnt**-1, **Wnt**-3a, **Wnt**-7a and **Wnt**-7b.
Further, dorsal spinal cord, which has been thought to mimic ureteric signaling in tubule induction induces **Wnt**-4 mutant as well as wild-type mesenchyme suggesting that spinal cord derived signal(s) most likely act by mimicking the normal mesenchymal action of **Wnt**-4.
These results lend addnl. support to the notion that **Wnt**-4 is a key auto-regulator of the mesenchymal to epithelial transformation that underpins nephrogenesis adding another level of complexity in the hierarchy of mol. events mediating tubulogenesis.

REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 20 OF 22 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:785854 HCAPLUS
DOCUMENT NUMBER: 130:165872
TITLE: Molecular mediators and models of **kidney tubule** induction
AUTHOR(S): Vainio, Seppo
CORPORATE SOURCE: Biocenter Oulu and Dep. Biochem., Univ. Oulu, Oulu, 90570, Finland

SOURCE: Trends in Glycoscience and Glycotechnology (1998), 10(55), 335-347
CODEN: TGGLEE; ISSN: 0915-7352
PUBLISHER: FCCA
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English/Japanese

AB A review with 66 refs. The developing kidney is a classic model system used to study mechanisms of organogenesis in mammals. Morphogenesis is regulated by epithelial-mesenchymal tissue interactions and involves inductive signaling across interactive tissue layers, ureter bud and metanephrogenic mesenchyme. As a response to induction a developmental program is activated in mesenchymal cells, and nephrons will develop as a result of mesenchymal-epithelial transformation and subsequent simple morphogenesis which follows the process. Mol. genetic experimentation where gene function has been disrupted by gene targeting has proven to be fruitful in revealing the mol. mechanisms of kidney development and attracted attention again to this model system. These expts. indicated that sequentially activated genes regulate organogenesis and that cell signaling between epithelial ureter and kidney mesenchymal tissue is a key morphogenetic regulator. Mol. mediators from such gene families as transcription factors, cell adhesion mols., kinases and secreted signaling mols. play an important role and are involved in the translation of cell behavior into morphogenesis. Recent data indicates that members of the **Wnt** gene family encoding secreted growth and differentiation factors act as classic tubule inducing signals. They are essential factors that control tubule induction and development in vitro and in vivo. A hypothetical model for some of the mol. mediators of tubule induction in vivo is presented.

REFERENCE COUNT: 66 THERE ARE 66 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 21 OF 22 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:739369 HCAPLUS
DOCUMENT NUMBER: 128:26947
TITLE: Method and compositions of a bioartificial kidney suitable for use in vivo or ex vivo
INVENTOR(S): Humes, H. David; Cieslinski, Deborah A.
PATENT ASSIGNEE(S): University of Michigan, USA
SOURCE: U.S., 28 pp., Cont.-in-part of U.S. Ser. No. 133,436.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5686289	A	19971111	US 1995-487327	19950607
US 5549674	A	19960827	US 1993-133436	19931008

PRIORITY APPLN. INFO.: US 1993-133436 A2 19931008
US 1992-844758 A2 19920302

AB A novel cell seeded hollow fiber bioreactor is described as a potential bioartificial kidney. Renal cells are seeded along a hollow fiber in a perfused bioreactor to reproduce the ultrafiltration function and transport function of the kidney. Maintenance of tissue specific function and ultrastructure suggest that this bioreactor provides an economical device for treating renal failure as well as studying renal tubululogenesis in vitro. Adult rabbit renal proximal tubule cells were grown in primary culture and the cultures were processed for passage by

treatment with 1.0 .mu.M all-trans retinoic acid and 10 nM epidermal growth factor for 24 h prior to passage. Cell plates were then treated with trypsin, followed by 0.1% soybean trypsin inhibitor and the cells were then removed and pelleted by centrifugation at which time various amts. of media were added to make the appropriate diln. of cells. A hollow fiber was layered with various matrix components including collagen type I, collagen type IV, laminin, and Matrigel, and then seeded with the renal proximal tubule progenitor cells. After 5-7 days of growth in the bioreactor, confluent growth along the inner surface was achieved with renal progenitor cells. An in vitro test system was established by connecting hollow fiber to a Harvard pump on the input side and to a collecting vial on the output side. Using this single pass perfusion system, various transport functions were assessed.

L14 ANSWER 22 OF 22 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1995:272463 HCAPLUS
DOCUMENT NUMBER: 122:52361
TITLE: Epithelial transformation of metanephric mesenchyme in the developing kidney regulated by **Wnt**-4
AUTHOR(S): Stark, Kevin; Vainio, Seppo; Vassileva, Galya; McMahon, Andrew P.
CORPORATE SOURCE: Dep. Molecular Cellular Biology, Harvard Univ., Cambridge, MA, 02138, USA
SOURCE: Nature (London) (1994), 372(6507), 679-83
CODEN: NATUAS; ISSN: 0028-0836
PUBLISHER: Macmillan Magazines
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The kidney has been widely exploited as a model system for the study of tissue inductions regulating vertebrate organogenesis. Kidney development is initiated by the ingrowth of the Wolfian duct-derived ureteric bud into the presumptive kidney mesenchyme. In response to a signal from the ureter, mesenchymal cells condense, aggregate into pretubular clusters and undergo an epithelial conversion generating a simple tubule. This then undergoes morphogenesis and is transformed into the excretory system of the kidney, the nephron. It is reported here that the expression of **Wnt**-4, which encodes a secreted glycoprotein, correlates with, and is required for, **kidney tubulogenesis**. Mice lacking **Wnt**-4 activity fail to form pretubular cell aggregates; however, other aspects of mesenchymal and ureteric development are unaffected. Thus, **Wnt**-4 appears to act as an autoinducer of the mesenchyme to epithelial transition that underlies nephron development.

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         (c)2003 Japan Science and Tech Corp(JST)
File 144:Pascal 1973-2003/Apr W3
         (c) 2003 INIST/CNRS
File 165:EventLine(TM) 1990-2003/Mar
         (c) 2003 Elsevier Science B.V.
File 340:CLAIMS(R)/US Patent 1950-03/Apr 24
         (c) 2003 IFI/CLAIMS(R)
File 342:Derwent Patents Citation Indx 1978-01/200282
         (c) 2003 Thomson Derwent
File 345:Inpadoc/Fam.& Legal Stat 1968-2003/UD=200316
         (c) 2003 EPO
File 351:Derwent WPI 1963-2003/UD,UM &UP=200324
         (c) 2003  Thomson Derwent
File 357:Derwent Biotech Res. _1982-2003/Apr W4
         (c) 2003 Thomson Derwent & ISI
File 434:SciSearch(R) Cited Ref Sci 1974-1989/Dec
         (c) 1998 Inst for Sci Info
File 440:Current Contents Search(R) 1990-2003/Apr 28
         (c) 2003 Inst for Sci Info
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Set    File     Items   Description
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        71         48
        73         85
        94          3
       144         17
       165          0
       340          2
       342          1
       345          0
       351         14
       357          5
       434          0
       440        186
S1                538   (WNT? OR HLDAT86) AND (KIDNEY?(5W)TUBUL? OR RENAL? OR
                    NEPHR? OR URO? HIV(W)1 OR HIV1 OR GLOMER? OR PYEL?)
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        35          1
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94	3	
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S3	2	S2 AND SULFATE?(W)GLYCOSAMINOGLYCAN?

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>>>No matching display code(s) found in file(s): 65, 165, 342, 345

3/AB/1 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE

10660132 EMBASE No: 2000135684
Bone morphogenetic protein 4 regulates the budding site and elongation of the mouse ureter
Miyazaki Y.; Oshima K.; Fogo A.; Hogan B.L.M.; Ichikawa I.
I. Ichikawa, Vanderbilt University Medical Center, MCN C4204, 21st and Garland Avenue, Nashville, TN 37232-2584 United States
AUTHOR EMAIL: iekuni.ichikawa@mcmail.vanderbilt.edu
Journal of Clinical Investigation (J. CLIN. INVEST.) (United States) 2000, 105/7 (863-873)
CODEN: JCINA ISSN: 0021-9738
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 34

In the normal mouse embryo, Bmp4 is expressed in mesenchymal cells surrounding the Wolffian duct (WD) and ureter stalk, whereas bone morphogenetic protein (BMP) type I receptor genes are transcribed either ubiquitously (Alk3) or exclusively in the WD and ureter epithelium (Alk6). Bmp4 heterozygous null mutant mice display, with high penetrance, abnormalities that mimic human congenital anomalies of the kidney and urinary tract (CAKUT), including hypo/dysplastic kidneys, hydroureter, ectopic ureterovesical (UV) junction, and double collecting system. Analysis of mutant embryos suggests that the kidney hypo/dysplasia results from reduced branching of the ureter, whereas the ectopic UV junction and double collecting system are due to ectopic ureteral budding from the WD and accessory budding from the main ureter, respectively. In the cultured metanephros deprived of sulfated glycosaminoglycans (S-GAGs),

BMP4-loaded beads partially rescue growth and elongation of the ureter. By contrast, when S-GAGs synthesis is not inhibited, BMP4 beads inhibit ureter branching and expression of Wnt11 , a target of glial cell-derived neurotrophic factor signaling. Thus, Bmp4 has 2 functions in the early morphogenesis of the kidney and urinary tract. One is to inhibit ectopic budding from the WD or the ureter stalk by antagonizing inductive signals from the metanephric mesenchyme to the illegitimate sites on the WD. The other is to promote the elongation of the branching ureter within the metanephros, thereby promoting kidney morphogenesis.

3/AB/2 (Item 1 from file: 351)
DIALOG(R)File 351:Derwent WPI

013507522
WPI Acc No: 2000-679466/200066
XRAM Acc No: C00-206615
Inducing kidney tubule formation in a post-natal mammal, involves administering a substantially pure Wnt polypeptide or its agonist
Patent Assignee: HARVARD COLLEGE (HARD)
Inventor: KISPERT A; MCMAHON A P; VAINIO S
Number of Countries: 021 Number of Patents: 001
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
WO 200061630	A1	20001019	WO 99US7745	A	19990408	200066	B

Priority Applications (No Type Date): WO 99US7745 A 19990408
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 200061630	A1	E	53	C07K-014/475	

Designated States (National): CA JP US
Designated States (Regional): AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE

Abstract (Basic): WO 200061630 A1
Abstract (Basic):

NOVELTY - Stimulating kidney tubule formation in a post-natal mammal involves administering a substantially pure Wnt polypeptide, Wnt agonist or a nucleic acid encoding the both. The Wnt polypeptide is not Wnt -11.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for an ex vivo mammalian kidney comprising a substantially pure exogenous Wnt polypeptide.

ACTIVITY - Cytostatic.

MECHANISM OF ACTION - Stimulator of kidney tubule formation; Wnt agonist; gene therapy.

USE - The method is useful for stimulating kidney tubule formation in an adult mammal suffering from a kidney disorder such as chronic renal failure, renal cell carcinoma, poly cystic kidney disease, chronic obstructive uropathy, and virus, especially HIV-1 induced nephropathy (claimed).

pp; 53 DwgNo 0/0
?

ANSWER 102 OF 156 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:323778 CAPLUS
DOCUMENT NUMBER: 125:41781
TITLE: **Glycosaminoglycan**-synthetic polymer conjugates
INVENTOR(S): Rhee, Woonza M.; Berg, Richard A.
PATENT ASSIGNEE(S): Collagen Corp., USA
SOURCE: U.S., 18 pp., Cont.-in-part of U.S. 5,324,775.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 18
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5510418	A	19960423	US 1993-146843	19931103
US 5162430	A	19921110	US 1989-433441	19891114
US 5324775	A	19940628	US 1992-907518	19920702
US 5304595	A	19940419	US 1992-998802	19921230
US 5306500	A	19940426	US 1993-110577	19930823
US 5376375	A	19941227	US 1994-177578	19940105
US 5523348	A	19960604	US 1994-292415	19940818
CA 2134745	AA	19950504	CA 1994-2134745	19941031
EP 656215	A1	19950607	EP 1994-117227	19941101
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, NL, SE				
JP 07278203	A2	19951024	JP 1994-271556	19941104
US 5543441	A	19960806	US 1995-427576	19950424
US 5470911	A	19951128	US 1995-433656	19950504
US 5476666	A	19951219	US 1995-434725	19950504

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US 1988-274071	B2	19881121
US 1989-433441	A2	19891114
US 1992-907518	A2	19920702
US 1992-930142	A3	19920814
US 1993-110577	A3	19930823
US 1993-146843	A	19931103
US 1994-177578	A3	19940105
US 1994-292415	A3	19940818

AB Pharmaceutically acceptable, nonimmunogenic compns. are formed by covalently binding **glycosaminoglycans** or derivs. thereof, to hydrophilic synthetic polymers via specific types of chem. bonds to provide biocompatible conjugates. Useful **glycosaminoglycans** include hyaluronic acid, the chondroitin sulfates, keratan sulfate, chitin and heparin, each of which is chem. derivatized to react with a hydrophilic synthetic polymer. The conjugate comprising a **glycosaminoglycan** covalently bound to a hydrophilic synthetic polymer may be further bound to collagen to form a three component conjugate having different properties. The hydrophilic synthetic polymer may be polyethylene glycol and derivs. thereof having an av. mol. wt. over a range of from about 100 to about 100,000. The compns. may include other components such as fluid, pharmaceutically acceptable **carriers** to form injectable formulations, and/or biol. active proteins such as growth factors or cytokines. The conjugates of the invention generally contain large amts. of water when formed. The conjugates can be dehydrated to form a relatively solid implant for use in hard tissue augmentation. The dehydrated, solid implant can further be ground into particles which can be suspended in a non-aq. fluid and injected into a

living being (preferably human) for soft tissue augmentation. Once in place, the solid implants or particles rehydrate and expand in size approx. three- to five-fold.

L2 ANSWER 103 OF 156 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:164957 CAPLUS
DOCUMENT NUMBER: 124:250384
TITLE: Low-molecular- weight heparin is responsible for the anti-Xa activity of Desmin 370
AUTHOR(S): Brieger, David; Dawes, Joan
CORPORATE SOURCE: Applied Research Group, Heart Research Institute, Sydney, Australia
SOURCE: Thrombosis and Haemostasis (1996), 75(2), 286-91
CODEN: THHADQ; ISSN: 0340-6245
PUBLISHER: Schattauer
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Dermatan sulfate does not catalyze the inactivation of factor Xa. However, the low-mol.-wt. (LMW) dermatan sulfate Desmin 370 has been shown to generate circulating anti-Xa activity following administration to humans. Using a single batch of Desmin 370, we measured 3 U/mg of anti-Xa activity by amidolytic assay in vitro. The material responsible for this activity had a lower mol. wt. range (6000 and 1800 Da) than Desmin 370 and was more highly sulfated than the bulk of the drug. Heparinase digestion of Desmin 370 eliminated 90% of the in vitro anti-Xa activity without significantly interfering with its ability to potentiate inactivation of thrombin by HCII, suggesting that the anti-Xa activity is not due to dermatan sulfate and is probably heparin. When 125I-labeled Desmin 370 together with 40 mg/kg **carrier** drug was administered i.v. to a rabbit, anti-Xa activity was readily detectable in the plasma for up to 10 h and had a longer half-life than the sulfated radiolabel. Most of this anticoagulant activity was recovered from the plasma by Polybrene affinity chromatog. and was probably a sulfated **glycosaminoglycan**. Administration of the heparinase-digested drug to a rabbit resulted in 70% less anti-Xa activity than the undigested drug. We conclude that Desmin 370 contains detectable quantities of biol. active low-mol.-wt. heparin, which is responsible for persistent anti-Xa activity following i.v. administration.

L2 ANSWER 113 OF 156 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1995:412924 CAPLUS
DOCUMENT NUMBER: 122:170233
TITLE: Growth factor and collagen composition for revitalizing scar tissue
INVENTOR(S): Berg, Richard A.; Rhee, Woonza Min
PATENT ASSIGNEE(S): Collagen Corp., USA
SOURCE: Eur. Pat. Appl., 10 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 637450	A2	19950208	EP 1993-112761	19930809
EP 637450	A3	19950405		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 07089867	A2	19950404	JP 1993-198671	19930810
CA 2103938	AA	19950205	CA 1993-2103938	19930812

PRIORITY APPLN. INFO.: US 1993-99241 19930804

AB A method is disclosed for remediation of scar tissue in a human or an animal by introducing into the scar tissue or adjacent tissue a remedial compn. comprising naturally occurring or synthetic growth factors and/or their active peptide segments. of naturally occurring and synthetic growth factors, and mixts. thereof. Typically the remedial compn. includes a biodegradable or nonbiodegradable support matrix material to provide for timed release of the bioactive material. Preferably, the support matrix is biodegradable and is selected from collagen, **glycosaminoglycan**, gelatin, albumin, hyaluronic acid, heparin, oxidized cellulose, dextran, polyglycolic acid, polylactic acid, polyanhydride, and mixts. thereof. To render the scar tissue less dense, to spatially expand the scar tissue fibrils, and to facilitate penetration of the remedial compn. into the scar tissue, a softening, expanding compn. is also introduced into the scar tissue prior to or simultaneously with the remedial compn. A preferred softening, expanding compn. includes .gtoreq.1 dried collagen-contg. polymer, .gtoreq.1 polymer hydrogel, and a nonaq. liq. **carrier** material. Thus, an injectable scar tissue-degrading compn. contained hyaluronic acid (3%, wt./vol.) and human gingival collagenase (1 mg/10 mL).